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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/773,356	02/05/2004	Leslie P. Weiner	23714-07992	6800

758 7590 04/19/2007
FENWICK & WEST LLP
SILICON VALLEY CENTER
801 CALIFORNIA STREET
MOUNTAIN VIEW, CA 94041

EXAMINER

EWOLDT, GERALD R

ART UNIT	PAPER NUMBER
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1644

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/773,356

Applicant(s)

WEINER ET AL.

Examiner

G. R. Ewoldt, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 8,9,12,14-19,23,26,28 and 30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 8,9,12,14-19,23,26,28 and 30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

1. Applicant's amendment, IDS, and remarks filed 2/07/07 are acknowledged.
2. Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 are pending and under examination.
3. In view of Applicant's amendment, the previous rejection under 35 U.S.C. 102 has been withdrawn. In particular Stinissen et al. does not teach the use T cells that target more than one different myelin protein. For the same reason the previous rejection under 35 U.S.C. 103(a) over Stinissen et al. alone has also been withdrawn. Additionally, the previous rejection under 35 U.S.C. 112, first paragraph, for lack of enablement has been withdrawn in view of the instant amendment wherein the T cells must be reactive to myelin proteins. Finally, the previous rejections under 35 U.S.C. 103(a) over Stinissen et al. in view of Correale et al. have been withdrawn and replaced by a new rejection. Accordingly the action has not been made FINAL.
4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 30 stands rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of:

A) The method comprising the specific steps set forth in Claim 30.

Note: including the new steps of the 2/07/07 amendment.

Applicant's arguments, filed 2/07/07 have been fully considered but they are not persuasive. Applicant argues that

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new amendments to the claim recite language from Example 1 of the specification and do not comprise the introduction of new matter.

A review of the example shows that Applicant has used some of the language of the example, but not all of it. For example, the first sentence of Example 1 discloses that it encompasses only a method of treating secondary progressive MS, yet the claim does not recite this limitation. Further, the Example discloses vaccination with 40×10^6 cells and vaccination intervals of 3 months or 6 weeks, limitations not found in the claim. Accordingly, the specification cannot support the method as claimed.

6. Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) ... T cells are cultured in the presence of whole bovine myelin proteins or synthetic human proteins ... (Claims 8 and 30).

B) ... T cells that respond to a plurality of different myelin proteins (Claim 11).

C) ... T cells are reactive to a plurality of different myelin proteins (Claim 23).

Regarding A), Applicant cites page 8 of the specification for support.

At page 8 the specification discloses PBMCs are cultured in the presence of cow myelin proteins or synthetic complete human proteins.

Regarding B) and C), Applicant cites pages 8 and 11 of the specification for support.

At page 8 the specification discloses PBMCs are cultured in the presence specific myelin antigens. Page 11 discloses a specific example in which PBMCs and myelin antigens are employed.

Applicant's arguments, filed 2/07/07 have been fully considered but they are not persuasive. Applicant argues that the specification teaches "T cells" at numerous cites.

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While the specification may disclose vaccines comprising T cells, the method of making the vaccine comprising T cells recited in the claims employs PBMCs.

7. The following are new grounds for rejection.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 rejected under 35 U.S.C. 103(a) each as being unpatentable over Stinissen et al. (1996) in view of Correale et al (1995) and the background teachings of the specification.

Stinissen et al. teaches a method of mediating an immune response comprising administering subcutaneously irradiation-attenuated T-cells derived from autologous peripheral mononuclear cells (comprising T cells) cultured in the presence of natural or synthetic human myelin proteins (see particularly page 503, T CELL VACCINATION IN MS).

The reference differs from the claimed invention only in that it does not teach the use of attenuated T cells that target more than one myelin protein and in that it does not teach the optimization of the claimed method as set forth in dependent Claims 16-19.

Correale et al. extends the teachings of Stinissen et al. regarding additional MS autoantigens. The reference teaches that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus, broadening the autoimmune response (see particularly page 1375, last paragraph - page 1376, first paragraph. The reference further teaches the use of bovine brain as a source of myelin proteins (see particularly page 1371, column 2).

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The background (Description of the Related Art) section of the specification further supports the teachings of Correale et al. See, for example, page 2 wherein the specification discloses "Presently, the myelin proteins thought to be the target of an immune response in MS include myelin basic protein (MBP), proteolipid protein (PLP), myelin associated glycoprotein (MAG), and myelin-oligodendrocyte glycoprotein (MOG). Also there is an increasing body of evidence that the T-cell receptor has extraordinary flexibility, allowing it to react to many different proteins (Brock R., K.H. Wiesmuller, et al. (1996) Proc. Natl. Acad. Sci. (USA) 93:13108-13113; Loftus D.J., Y. Chen, et al. (1997) J. Immunol. 158:3651-3658)." The specification additionally discloses, "In both EAE and MS, myelin basic protein (MBP), proteolipid protein (PLP), and MOG are thought to be the main target antigens for autoreactive T-cells (Brostoff S.W. and D.W. Mason (1984) J. Immunol. 133:1938-1942; Tabira and Kira, 1992). Myelin associated glycoprotein (MAG) may be important in MS but does not produce EAE in experimental models."

From the teachings of the references it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to perform the method of administering attenuated T cells, as taught by Stinissen et al., employing attenuated T cells autoreactive to multiple human myelin antigens. One of ordinary skill in the art at the time the invention was made would have been motivated to employ attenuated T cells autoreactive to multiple myelin antigens given the teachings of Stinissen et al. that MBP is not the only autoantigen candidate in MS, extended by Correale et al. that as MS develops, myelin breakdown exposes additional myelin antigens (besides MBP) to autoreactive T cells, thus broadening the autoimmune response, and the background teachings of the specification that multiple protein antigens are targeted in MS. One of ordinary skill in the art at the time the invention was made would also have been motivated to employ myelin proteins obtained from bovine as a convenient source of said proteins given the teachings of Correale et al. of the availability of said source. Further, the choice of dosage (Claim 17), and timing (Claim 16), would have fallen well within the purview of the skilled artisan at the time of the invention. Regarding the increasing of the dosages as set forth in Claims 18 and 19, one of ordinary skill in the art at the time the invention was made would have been well aware of the concept of increasing dosage if no response is obtained up to the point of efficacy or

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adverse reaction. These limitations do not render the claimed method patentably distinct.

Applicant's arguments to a similar previous rejection, filed 2/07/07 have been fully considered but they are not persuasive. Applicant argues that the prior art does not teach the production of the attenuated T cells administered in the claimed method by the method of the instant claims.

A review of the instant claims shows that they comprise a method of treating MS employing a product-by-process. In such instances the process by which the product is produced is considered irrelevant to the method of treating unless said process results in a product that would comprise patentably distinct treatment properties. In the instant case the claims are simply read as reciting a method of treating MS by administering attenuated T cells reactive to a plurality of different bovine or human myelin proteins.

Applicant argues that Stinissen et al. teaches away from the claimed method.

A review of the reference reveals only that highly purified T cells are necessary for use in the treatment of MS. There is no teaching that said purified T cells cannot be produced.

Applicant cites Van der Aa, A., et al. (2003) as teaching that it would be almost impossible to generate T cell clones specific for three different myelin antigens.

A review of the reference discloses that the statement regarding the difficulty of generating T cell clones specific for three different myelin antigens is made in the Introduction section of the reference with no explanation. Indeed, the next paragraph teaches that the authors were able to do that very thing, i.e., the generation of sufficient T cells for vaccination, with no particular difficulty. Accordingly, the isolated statement regarding difficulty in generating T cell clones would not lead the skilled artisan to doubt the expectation of success with the claimed method.

10. Claims 8, 9, 12, 14-19, 23, 26, 28, and 30 are rejected under 35 U.S.C. 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in

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the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically: "T cells ... prepared by selecting and expanding human T-cells that respond to a plurality of different myelin proteins ...".

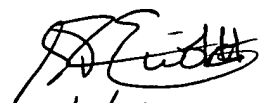
Applicant cites original Claims 11 and 13, and pages 8 and 11 of the specification in support.

A review of the cites does not reveal T cells prepared by the claimed method. As set forth previously, the specification discloses the culturing of PBMCs and not just T cells.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

13. **Please Note:** Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.


4/13/07

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600